Incidence of Tuberculosis Disease among Household Contacts of Adult Pulmonary Tuberculosis Patients in India-CTRIUMPH A Multi Centric Cohort Study


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Background

• WHO’s new End TB Strategy 2035
  – 90% reduction in TB incidence
  – 95% reduction in TB deaths

• Preventing development of active TB
  – Break the cycle of transmission
  – Decrease the overall burden of TB worldwide [JuanPabloMillet 2013]

• Household Contacts (HHC) of Pulmonary TB (PTB) patients
  – High risk for developing TB disease [WHO 2012,RNTCP TOG2016]
  – High quality estimates of TB incidence are needed for TB vaccine trials focused on prevention of disease (POD)

• India has 27% of world’s TB burden and therefore an important place to estimate incidence
Objective

• *Primary Objective:* To estimate the incidence of TB disease among household contacts of newly diagnosed adult PTB patients started on TB treatment in India

• *Secondary Objective:* To determine the factors associated with incidence of TB disease among these household contacts
Methods

• **Study Design:** Multi centric Cohort Study (CTRIUMPH Gupte et al BMJ Open 2016)

• **Study Settings:** Chennai [NIRT] and Pune [BJMC]

• **Study Period:** March 2014- December 2017
  – Recruitment completed and follow up ongoing

• **Active TB Cohort (Cohort A):** Adults with newly diagnosed PTB starting RNTCP Category I treatment [2EHRZ3/4RH3]

• **Household Contact cohort (Cohort B):** defined to include all adults and children living in the same house as the adult (18+yrs) PTB participant during the 3 months prior to diagnosis of TB
  – followed for 24 months and assessed for TB at baseline, 4-6 months, 12, 18 and 24 months
Outcome

- **Incident TB** defined as occurrence of **TB disease** >1 month to 24 months
- **Prevalent TB** defined as occurrence of **TB disease** within 1 month of initial household screening
- A **case of TB disease** diagnosed on the basis of any of the following:
  - Microbiologically confirmed [smear, CBNAAT, culture]
  - Clinically diagnosed [X-ray abnormalities, histopathology and/or clinical signs suggestive of TB]
- **TB infection positive** defined as any HHC positive by TST >5 mm and/or QuantiFERON Gold In Tube test (QGIT) ≥0.35 IU/mL.
Data Collection and Analysis

• Institutional Ethics Committee Approvals at NIRT, BJGMC, JHU
• Trained study staff collected data
  – Pre-tested questionnaire after written Informed Consent
• Data analyzed using STATA 15
• Interim analysis
• Incident rate ratios and 95% CIs
• Kaplan-Meier curves for occurrence of TB disease
• Adjusted Relative Risk (aRR) for TB incidence
  – Poisson regression adjusted for the household clustering and factors significant at 20% level by univariate analysis
Index adult Pulmonary TB Patients CohortA recruited N=504

Number of HHC Screened N=1930 (3.8 per PTB Case)

Not willing to Participate n=879(45.5%)

Number of HHC Enrolled at Baseline N=1051

Prevalent TB at Baseline n=26

HHC without TB at Baseline Evaluation n=1025

Bacteriologically Confirmed =9 Clinically Diagnosed=17

Out of 1025, 839 had completed a minimum of 12 Months of Follow-up
HHC-Demographic Characteristics [N=839]

- Non Smokers: 92.1%
- Literate: 88.7%
- Non Alcoholics: 86.7%
- Employed: 58.2%
- Male: 53.5%
- Age Group >45: 51.5%
HHC- Clinical Characteristics [N=839]

- BMI>18: 67.3%
- BCG Scar Present: 54.2%
- TST + (Baseline): 51.8%
- Quantiferron Gold In Tube Test+(Baseline): 49.1%
- Diabetic: 32.9%
- HIV: 1.8%
HHC - Behavioural Characteristics [N=839]

- No h/o TB Contacts outside Household: 91.2%
- Average time Spent with index TB patients per day (>6hrs): 85.9%
- Sharing more than 2 meals with Index TB patients per day: 68.9%
- Sleeping in the same room with Index Patients after diagnosis: 68.4%
- Index Patient being a primary care provider: 20.9%
Number of HHC eligible for follow-up for incident TB Disease N= 1025

Number of HHC Evaluated at 4th M N= 840/977 (86%)

Number of HHC Evaluated at 6th M N= 842/946 (89%)

Number of HHC Evaluated at 12th M N = 790/840 (94%)

Number of HHC Evaluated at 18th M N = 606/681 (89%)

Number of HHC Evaluated at 24th M N = 507/545 (93%)

Incident TB at 4th M n = 4

Incident TB at 6th M n = 5

Incident TB at 12th M n = 2

Incident TB at 18th M n = 2

Incident TB at 24th M n = 3

Incident TB Cases =16
Bacteriologically Confirmed =5
Pulmonary TB=13
Clinically Diagnosed=11
Extra Pulmonary TB=3
## Incidence Rate Ratio of TB by age and gender

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
<th>Number of TB cases</th>
<th>Person-Years of Follow-up</th>
<th>Rate (95% CI)/1000 PYF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age Group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6</td>
<td>68</td>
<td>1</td>
<td>106</td>
<td>9.4 (1.32 - 66.71)</td>
</tr>
<tr>
<td>6-14</td>
<td>156</td>
<td>6</td>
<td>255</td>
<td>23.53 (10.57 - 52.37)</td>
</tr>
<tr>
<td>14-25</td>
<td>183</td>
<td>2</td>
<td>310</td>
<td>6.46 (1.61 - 25.82)</td>
</tr>
<tr>
<td>&gt; 25</td>
<td>432</td>
<td>7</td>
<td>714</td>
<td>9.81 (4.67 - 20.57)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>392</td>
<td>10</td>
<td>731</td>
<td>15.29 (8.23 - 28.42)</td>
</tr>
<tr>
<td>Female</td>
<td>447</td>
<td>6</td>
<td>654</td>
<td>8.21 (3.69 - 18.27)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>839</td>
<td>16</td>
<td>1385</td>
<td>11.55 (7.08 - 18.86)</td>
</tr>
</tbody>
</table>
## Incidence Rate Ratio of TB by Infection Status

<table>
<thead>
<tr>
<th>Test</th>
<th>N</th>
<th>Number of TB cases</th>
<th>Person-Years of Follow-Up (PYF)</th>
<th>Rate (95% CI)/1000 PYF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TST (5 mm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pos.</td>
<td>435</td>
<td>7</td>
<td>727</td>
<td>9.64 (4.6 - 20.22)</td>
</tr>
<tr>
<td>Neg.</td>
<td>377</td>
<td>6</td>
<td>618</td>
<td>9.71 (4.36 - 21.61)</td>
</tr>
<tr>
<td><strong>Quantiferon Gold in Tube Test</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pos.</td>
<td>412</td>
<td>9</td>
<td>698</td>
<td>12.9 (6.71 - 24.8)</td>
</tr>
<tr>
<td>Neg.</td>
<td>346</td>
<td>6</td>
<td>569</td>
<td>10.53 (4.73 - 23.45)</td>
</tr>
<tr>
<td><strong>TST (5 mm) &amp; Quantiferon Gold in Tube Test</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T+ Q+</td>
<td>252</td>
<td>5</td>
<td>425</td>
<td>11.77 (4.9 - 28.28)</td>
</tr>
<tr>
<td>T+ Q-</td>
<td>148</td>
<td>2</td>
<td>248</td>
<td>8.05 (2.01 - 32.21)</td>
</tr>
<tr>
<td>T- Q+</td>
<td>148</td>
<td>2</td>
<td>256</td>
<td>7.83 (1.96 - 31.3)</td>
</tr>
<tr>
<td>T- Q-</td>
<td>190</td>
<td>4</td>
<td>306</td>
<td>13.06 (4.9 - 34.8)</td>
</tr>
</tbody>
</table>
Timing of TB Disease Incidence

Kaplan-meier curve by Year

Year 1: 11 TB, Incidence Rate: 84(46-151)
Year 2: 5 TB, Incidence Rate: 5(2-10)

p < 0.001
Factors associated with development of Incident TB in HHC of PTB patients

- Age of < 6 years
- Age of 6 - 15 years
- Age of 15 - 45 years
- Age of > 45 years
- Female Gender
- Male Gender
- Unemployed
- Employed
- BMI > 18
- BMI < 16
- BMI (16 - 18)
- Presence of BCG Scar
- Absence of BCG Scar
- LTBI -ve
- LTBI +ve
- Average Time Spent with Index per Day < 12 hrs
- Average Time Spent with Index per Day ≥ 12 hrs
- Sharing Meals - 1 or Less
- Sharing Meals - 2
- Sharing Meals - 3 or More
- Non-Care Giver
- Care Giver to Index
- Index Cough < 8 weeks
- Index Cough > 8 weeks
- Absence of Cavity
- Presence of Cavity
- Index Culture Negative
- Index Culture Positive
Comparison with Systematic Review and Meta-analysis on Contact investigation for TB

<table>
<thead>
<tr>
<th>Measure</th>
<th>Fox, Gregory J., et al. % (95% CI)</th>
<th>Our Study % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident TB Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>1.6 (0.8–3.3)</td>
<td>1.4 (0.7-2.3)</td>
</tr>
<tr>
<td>Year 2</td>
<td>0.4 (0.2–0.9)</td>
<td>0.6 (0.3-1.4)</td>
</tr>
<tr>
<td>Co-Prevalent TB Disease</td>
<td>4.1 (2.6–6.4)</td>
<td>2.5 (1.7-3.6)</td>
</tr>
</tbody>
</table>

Recommendations for investigating contacts of persons with infectious tuberculosis in low- and middle-income countries.WHO.2012
Conclusion

• Majority of Incident TB disease among HHC
  – Occurs within the first 12 months of index TB patient diagnosis

• Higher Risk for TB disease Incidence among HHC of PTB
  – Age group between 6-15 years
  – Male Gender
  – Employed
  – Increased exposure to Index patient per Day
  – Longer Index Patient Cough Duration
Recommendation

• Systematic implementation of Contact Screening
  – All age groups of the HHC of PTB patients
  – Close follow up for TB disease break down

• Inclusion of 6-15 years age group for chemoprophylaxis

• Health Education
  – Cough Hygiene for index TB patients
  – To increase awareness about TB symptoms
  – For early diagnosis of TB cases to prevent transmission
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Thank you